Drug Coverage Policy

Effective Date.....10/1/2024
Coverage Policy Number.....IP0608
Policy Title.....Xphozah

Nephrology – Xphozah

- Xphozah® (tenapanor tablets - Ardelyx)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

OVERVIEW
Xphozah, a sodium hydrogen exchanger 3 (NHE3) inhibitor, is indicated to reduce serum phosphorus in adults with chronic kidney disease (CKD) on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy.[1]

Efficacy
The efficacy of Xphozah was evaluated in three pivotal trials (PHREEDOM, BLOCK, and AMPLIFY) in patients with CKD on dialysis with hyperphosphatemia. In the PHREEDOM and BLOCK trials, patients had a serum phosphorus level of at least 6.0 mg/dL to 10.0 mg/dL.[1] In the AMPLIFY trial,

patients had a serum phosphate level of 5.5 to 10 mg/dL. All patients had been on maintenance dialysis for ≥ 3 months. In all three pivotal trial, the primary endpoint, which was the difference in the mean change in serum phosphate levels in patients taking Xphozah vs. placebo was statistically significant.

Guidelines
The Kidney Disease Improving Global Outcomes (KDIGO) published a 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of CKD-mineral and bone disorder (CKD-MBD), which is a selective update of the prior CKD-MBD guideline published in 2009.[2] Xphozah is not mentioned in the guidelines. The classification of CKD in these guidelines are based upon glomerular filtration rate (G1 to G5) and albuminemia (A1 to A3); G5D represents kidney failure on dialysis. Treatment options for hyperphosphatemia include diet modification, phosphate-lowering therapy, and intensified dialysis for patients with CKD stage G5D. The following are recommendations in patients with CKD G3a to G5D. Elevated phosphate levels are suggested to be lowered toward the normal range (Grade 2C recommendation). The guideline update does not provide the reference value of normal range. Decisions about phosphate-lowering treatment is suggested to be based on progressively or persistently elevated serum phosphate (not graded). The broader term "phosphate-lowering" treatment is used instead of phosphate-binding agents since all possible approaches (i.e., phosphate binders, diet, dialysis) can be effective, which is change from the 2009 guidelines.[3]

Medical Necessity Criteria

Xphozah is considered medically necessary when the following criteria are met:

FDA-Approved Indications

1. **Hyperphosphatemia in Chronic Kidney Disease.** Approve for 12 months if the patient meets the following (A, B, C, D, E and F):
   - **A.** Patient is ≥ 18 years of age; AND
   - **B.** Patient has chronic kidney disease (CKD); AND
   - **C.** Patient has been on maintenance dialysis for ≥ 3 months; AND
   - **D.** Patient's serum phosphate level is ≥ 5.5 mg/dL and <10.0 mg/dL; AND
   - **E.** Patient meets one of the following (i or ii):
     - **i.** Patient meets both of the following (a and b):
       - **a)** Patient has tried at least two phosphate binders; AND
         Note: Examples of phosphate binders include: sevelamer, lanthanum, ferric citrate, and sucroferric oxyhydroxide, calcium carbonate, and calcium acetate.
       - **b)** Patient had an inadequate response and/or intolerance to at least two phosphate binders; OR
     - **ii.** Patient meets one of the following (a or b):
       - **a)** Patient has a contraindication to at least two phosphate binders; OR
         Note: Contraindication to phosphate binders includes bowel obstruction, iron overload, or hypercalcemia.
       - **b)** Patient meets both of the following (1 and 2):
         - **1)** Patient had an inadequate response and/or intolerance to at least one phosphate binder; AND
         - **2)** Patient has a contraindication to at least one phosphate binder.
           Note: Contraindication to phosphate binders includes bowel obstruction, iron overload, or hypercalcemia.
   - **F.** The medication is prescribed by or on consultation with a nephrologist.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

References

1. Xphozah® tablets [prescribing information]. Waltham, MA: Ardelyx; October 2023.
2. Ketteler M, Block G, Evenepoel P, et al. Diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder: synopsis of the kidney disease: improving global outcomes 2017 clinical practice guideline update. *Ann Intern Med*. 2018; 168 (6): 422-430.
3. Ketteler M, Block G, Evenepoel P, et al. Executive summary of the 2017 KDIGO Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) Guideline Update: what's changed and why it matters. *Kidney Int*. 2017; 92(1):26.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	5/1/2024
Annual Revision	No criteria changes	10/1/2024

The policy effective date is in force until updated or retired.